Complete Summary

GUIDELINE TITLE

Nephropathia epidemica (NE).

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Nephropathia epidemica (NE). In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2007 Apr 4 [Various].

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Makela S. Nephropathia epidemica (NE). In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2006 May 4 [various].

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Nephropathia epidemica (NE)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Nephrology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients with suspected or known nephropathia epidemica (NE)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of signs and symptoms
2. Laboratory evaluations including basic hematological parameters (hemoglobin or hematocrit, leucocyte count, and thrombocyte count), C-reactive protein, serum creatinine, and urinalysis, with chest x-ray, electrocardiogram, and ultrasonography of the kidneys, as indicated
3. Serologic testing (immunofluorescence and/or enzyme-linked immunological techniques) for antibodies to Puumala hantavirus

Treatment/Management

1. Fluid therapy
2. Analgesics
3. Monitoring
4. Hospital care
5. Follow-up in one week to one month

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. **Quality of Evidence: High**

Further research is very unlikely to change confidence in the estimate of effect

- Several high-quality studies with consistent results
- In special cases: one large, high-quality multi-centre trial

B. **Quality of Evidence: Moderate**

Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

- One high-quality study
- Several studies with some limitations

C. **Quality of Evidence: Low**

Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

- One or more studies with severe limitations

D. **Quality of Evidence: Very Low**

Any estimate of effect is very uncertain.

- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Essentials

- Nephropathia epidemica (NE) is an acute infectious disease in Northern Europe caused by Puumala (PUU) hantavirus (Vapalahti et al., 2003; Muranyi et al., 2005).
- The clinical picture varies from symptomless to severe.
- NE should be suspected in patients with acute febrile disease who are found to have thrombocytopenia, haematuria, and proteinuria.
- Infection confers lifelong immunity.

Epidemiology

- Hantaviruses are enveloped RNA-viruses found all over the world.
- In Europe and Asia, hantaviruses cause haemorrhagic fever with renal syndrome (HFRS). On the American continent, the so called hantavirus pulmonary syndrome (HPS) is encountered.
- The Puumala hantavirus is transmitted to humans by the excretions of a bank vole (*Clethrionomys glareolus*), apparently by inhalation through the airways.
- The majority of cases occur between August and January.
- NE has not been shown to transmit between humans.
- Two thirds of the patients are men.
- In children, the disease is found rather seldom and the clinical course is usually milder than in adults.

Clinical Picture

- The most common symptoms and signs of NE are presented in the table below.

Table. The Most Common Symptoms and Signs of NE (Mustonen et al., 1994; Lahdevirta 1971; Settergren et al., 1989)

Symptom	Frequency (%)
Fever	98–100
Headache	62–90
Back ache	54–82
Abdominal pain	43–67
Nausea/vomiting	58–84
Myalgia	27–69
Oliguria (<400 mL/24 hours)	54–70
Polyuria (>2,000 mL/24 hours)	97
Visual disturbances	12–36
Petechiae	1–12
Diarrhoea	12–20
Cough	6–32

Laboratory Findings

- The most common laboratory findings in NE are presented in the Table below.

Table. The Most Common Laboratory Findings in NE (Mustonen et al., 1994; Lahdevirta 1971; Settergren et al., 1989)

Finding	Frequency (%)
Proteinuria	94–100
Haematuria	58–87
Increased serum creatinine*	86–96
Thrombocytopenia	75
Increased C-reactive protein (CRP)	52–60
Increased liver enzymes	41–60
Hypoalbuminaemia/hypoproteinaemia	24–64
Leucocytosis >10.0 x 10^9/L	23–57

*Usually 3 to 7 days after the onset of fever

- In some patients, increased haemoglobin or haematocrit values are found in the acute phase; later on, anaemia is common.
- Disturbances in electrolyte balance are common but their clinical significance is usually marginal.

Chest X-ray

- Abnormal chest x-ray findings are present in one third of hospitalized adult patients: pleural effusion, parenchymal infiltrates, and occasionally pulmonary oedema (Kanerva et al., 1996)

Electrocardiogram (ECG)

- Nonspecific, transient changes are found in a half of the hospitalized patients: ST-depression and T-wave inversions.

Ultrasonography of the Kidneys

- Enlarged kidneys with pleural, pericardial, or perirenal effusions may be found in ultrasound examination (Paakkala et al., 2002).

Diagnosis

- Diagnosis is based on typical clinical picture and serology.
- First-line studies in an outpatient unit include basic haematological parameters (haemoglobin or haematocrit, leucocyte count, and thrombocyte count), CRP, serum creatinine, and urinalysis.
- Antibodies to Puumala hantavirus
    - Diagnosis is confirmed with one serum sample using immunofluorescence and/or enzyme-linked immunological techniques.
    - If the result is negative and less than 6 days have elapsed since the onset of symptoms, the result should be confirmed with another sample.

Differential Diagnosis

- Other viral infections
- Acute bacterial infections (septicaemias, pyelonephritis)
- Other types of acute nephritis

Course of the Disease

- There are typical phases in the clinical course; however, they are not seen in all patients.
    1. Febrile phase (high fever, pains, general symptoms)
    2. Hypotensive phase (haemoconcentration, shock)
    3. Oliguric phase (renal failure, fluid retention)
    4. Polyuric phase (excessive urinary secretion)
    5. Convalescence phase (days, weeks, or even months)

- About 5% of hospitalized patients need dialysis.
- Severe course of the disease is associated with HLA-B8 and DR3 (Mustonen et al., 1996).

Treatment

- Mild cases may be treated in primary health care on an outpatient basis or on the observation ward of a health centre.
    - Fluid therapy
    - Analgesics
        - Paracetamol is a suitable analgesic; non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided because they impair renal function.
    - Patient's condition and laboratory parameters should be frequently monitored: depending on the clinical picture, the situation is assessed every 2 or 3 days or even daily if necessary.
- Indications for referral to for hospital care
    - Deteriorated general condition
    - Dehydration
    - Fluid retention
    - Renal failure (serum creatinine >150 micromol/L), oliguria
    - Uncertain diagnosis

Follow-up

- A control visit is recommended one week to one month after hospital discharge depending on the severity of the disease, especially if acute renal failure was associated with NE. The clinical condition and the laboratory parameters should be normalized one month after the onset of the disease.
- Fatigue may continue several weeks after the acute phase.

Prognosis

- Mortality with NE is low (<0.1%).
- Long-term prognosis with the disease is good (Miettinen et al., 2006).
- Panhypopituitarism and chronic glomerulonephritis have been described as rare long-term complications of NE.

Prevention

- There is no research evidence on the possible benefit from a respirator mask in the prevention of NE.
- For the time being, there is no vaccine against the Puumala virus.

Definitions:

Levels of Evidence

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis and appropriate management/treatment of nephropathies epidemica (NE)

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jun 21 (revised 2007 Apr 4)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Satu Makela

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 30, 2005. This NGC summary was updated by ECRI on August 7, 2006, and on January 3, 2008.

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Date Modified: 9/22/2008